The Influence of Monetary Reward Contingency on Response Strategy in an fMRI Decision-Making Task

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ABSTRACT

BACKGROUND: Previous functional imaging studies investigating the neural correlates of financial decision-making have suggested that subjects may adopt different response strategies depending on the degree of reward/punishment they received. We wanted to investigate whether there is a strategic difference, and whether a shift in response strategy relates to differential BOLD fMRI activation.

METHOD: A within-subject, block design using a modified continuous performance task divided into a reward and punishment session was used to examine fMRI BOLD responses in 18 healthy volunteers. Six black and white line drawings were simultaneously presented to the participants for 300 ms. They were to determine if one of the six drawings depicted an animal or insect. The background colour of the screen indicated whether they could win NOK 3 and lose NOK 1 for correct and incorrect responses, or whether there were no monetary consequences. In the punishment session, the amounts that could be won or lost were reversed. Strategic flexibility was measured as a difference in response bias ($\ln\beta$) between monetary contingencies.

RESULTS: Both the reward and the punishment block yielded significant activations in the bilateral: ventral striatum, anterior insula, anterior cingulate and the orbitofrontal cortex compared to blocks without monetary consequences. Participants adopted a more liberal response bias in the punishment block than in the no-punishment block. Those who showed greater response-strategy flexibility in the punishment session had increased dorsolateral prefrontal cortex, sensory motor area and ventral lateral orbitofrontal cortex activation compared to those who were less strategically flexible. There was no difference in activations between the reward and punishment blocks.

CONCLUSIONS: These findings suggest that there are differences in response strategies in studies using financial decision-making models and that these differences manifest as differential activation patterns that may need to be modelled or controlled for in future studies.

INTRODUCTION

NEUROECONOMICS

Everyday, people make hundreds of different decisions. These range from the mundane decision of what to cook for dinner, to the more profound decision of what career path to choose. No matter the gravity of the decision to be made, the chosen outcome guides subsequent behaviour. Animal research has demonstrated that stimuli that are either rewarding or predict reward will elicit approach behaviour (Berridge & Robinson, 1998). Conversely, stimuli that are punishing or predict punishment will result in avoidance behaviour (Berridge, 2007). Humans behave the same way - they approach reward and avoid punishment. They also have the mental flexibility to adopt different strategies in the decisions they make. This is evident when two people confronted with an identical choice scenario make different decisions, or when a single person with the same choice scenario, but in a different context, makes two different decisions.

While people exercise a degree of flexibility in the decision-making strategies they use, the choices people make are still predictable enough that they can be modelled mathematically. Expected Utility Theory (von Neumann & Morgenstern, 1944) suggests that the expected utility of a decision (U) is the sum of its probability weighted (p) outcomes [$u(x)$]:

$$U(p_1,x_1;\ldots;p_n,x_n) = p_1u(x_1)+\ldots+p_nu(x_n)$$

According to this theory, people will choose the decision which maximises utility. Consider, for example, the decision between A) a 50% chance of winning 500Kr and a 50% chance of winning nothing; and B) a 100% chance of winning 240Kr:

$$A(p_1,x_1;\ p_2,x_2) = 0.5(500Kr) + 0.5(0) = 250Kr$$

$$B(p_1,x_1;\ p_2,x_2) = 240Kr$$

Since the expected utility of A is 250Kr and the expected utility of B is 240Kr, Expected Utility Theory predicts that A will be chosen over B; however, it is not. Prospect Theory (Kahneman & Tversky, 1979) terms this "the certainty effect," whereby outcomes obtained with certainty are more heavily weighted than those which are uncertain. To account for this and other incongruencies in Utility Theory, Prospect Theory suggests that there is a decision weight (π) associated with the probability value which affects the over-all value of a decision:

$$V(x, p; y, q) = \pi(p)v(x) + \pi(q)v(y)$$

While these two theories do differ, they share the conception that expected reward value is a combination of the magnitude of the reward and the expected risk involved in obtaining it.

Expected reward value = reward magnitude x expected risk

Since the decisions that people make play such a large role in their subsequent behaviour, a large body of research has focused on investigating how the decision-making process is represented in the human brain. The advent of functional magnetic resonance imaging (fMRI) and the idea that different components of the decision-making process – risk, magnitude, and value – are represented in different areas of the human brain has led to the creation of a relatively new scientific field known as neuroeconomics. This field investigates the neural mechanisms that underlie financial decision-making.

VENTRAL STRIATUM

Many of the early neuroeconomic studies focused on the role the human ventral striatum plays in decision-making. The interest in this area of the brain was a direct result of the large body of animal research implicating the mesolimbic dopaminergic pathway in reward processes (Schultz, 1997; Schultz, 1998). Animal studies demonstrated that blocking striatal dopamine (DA) diminished behavioural response for reward, while increasing striatal DA enhanced reward response behaviour (Ikemoto & Panksepp, 1999). Disruption and enhancement of ventral striatal DA seemed to directly affect an item's worth. This suggested that a reward's value was represented in the ventral striatum. Similarly, human positron emission tomography (PET) studies found that there was a link between ventral striatal DA release and the receipt of monetary reward (Thut et al., 1997; Zald et al., 2004). Functional MRI studies showed that the ventral striatum was involved in processing primary reward (Berns et al., 2001), the rewarding properties of drugs of abuse (Breiter et al., 1997), and monetary reward (Delgado et al., 2000; Knutson et al., 2000; Knutson et al., 2001a; Knutson et al., 2001b; Breiter et al., 2001; Ernst et al., 2004; Jensen et al., 2007). It was further demonstrated that monetary reward related activation was proportional to the value of the reward that could be gained (Elliott et al., 2000; Knutson et al., 2001a; Knutson et al., 2003). Ventral striatal activation to reward magnitude also appeared to be independent of reward

probability (Knutson et al., 2005) suggesting that the ventral striatum encodes reward magnitude, but not risk.

There are several problems with the idea that the ventral striatum represents reward magnitude. First, studies have shown that the ventral striatum responds to salient non-rewarding events in both animals (Horvitz, 2000) and humans (Zink et al., 2003; Zink et al., 2004). Second, fMRI studies have shown that aversive as well as appetitive stimuli activate the ventral striatum (Jensen et al., 2003; Levita et al., 2008). Two theories have tried to account for these findings. One suggests that the ventral striatum codes for both the valence and salience of stimuli (Cooper & Knutson, 2008). The other proposes that the ventral striatum encodes an error-prediction signal between the expected value of a reward and the value of the reward that is actually received (McClure et al., 2003; Pessiglione et al., 2006; Jensen et al., 2007; Menon et al., 2007; Seymour et al., 2007; Hare at al., 2008).

A prediction-error arises when the outcome of a decision results in a different value than what was expected. For example, if one predicts that a particular decision will lead to a 500Kr reward, but what is received is 400Kr or 600Kr reward instead, a negative or a positive prediction-error has respectively occurred. In keeping with animal studies that have found that midbrain dopamine modulates a prediction-error signal (Schultz, 1997; Schultz, 2002), functional MRI studies have demonstrated that the ventral striatum responded to prediction-error regardless of whether the stimulus was aversive or appetitive (Jenson et al., 2007). It has also been shown that there is a functional division of the ventral striatum with an anterior portion coding financial gain prediction-errors, and a more posterior portion coding financial loss prediction-errors (Seymour et al., 2007). A prediction-error signal is important in the decision-making process because it signals that one's calculation of expected reward value from reward magnitude and expected risk is incorrect. This should lead to an updating of magnitude and risk valuation and will possibly alter decision-making strategy and behaviour.

It has been found that ventral striatal activation increases with both increasing reward magnitude and increasing reward probability (Abler et al., 2006; Yacubian et al., 2006). This finding implicates the ventral striatum as the region that integrates the reward magnitude and risk components of a decision option, and represents their combined contribution as reward value (Knutson & Bossaerts, 2007). This finding, along with the prediction-error literature, suggests that the ventral striatum is involved in coding the value of a decision-outcome as

well as the prediction-error that results if there is a disparity between the expected and obtained value of that decision.

ORBITOFRONTAL CORTEX

One of the problems using fMRI to separate the brain regions that code for expected magnitude, expected risk, expected value and prediction-errors is that activations in these regions are highly correlated (Hare et al., 2008). Using a study that separated reward magnitude and prediction-error, Hare et al. (2008) replicated the finding that prediction error is coded in the ventral striatum, and in addition found that reward magnitude was represented in the medial orbitofrontal cortex (OFC). Interestingly, lateral OFC activation positively correlates with punishment magnitude while medial OFC activation positively correlates with reward magnitude and that there is a reciprocal relationship between the two areas – when lateral OFC activation increases, medial OFC activation decreases (O'Doherty, et al., 2001), suggesting that the magnitude of both rewards and punishments are represented in the OFC. These finding complement the animal literature which suggests that the value of primary rewards was represented in the OFC (Rolls, 2000), and that OFC activity increased as the relative value of a reward increased (Padoa-Schioppa & Assad, 2006).

In keeping with findings from the animal literature, functional MRI studies have found that the OFC coded relative and not absolute value of reward magnitude (Watanabe, 1999; Elliott et al., 2003; Knutson et al., 2003; Elliott et al., 2008). It has also been reported that patients with OFC damage were inconsistent in how they coded relative value (Fellows & Farah, 2007). In a value-based preference study, participants were presented with pairs of items, for example: an apple (A), a brown coloured square (B), a carrot (C), and indicated which item in a pair they preferred over the other. If A was preferred to B and B was preferred to C, then they should prefer A over C. A preference of C over A is inconsistent. Patients with OFC damage had significantly more inconsistent preferences than controls. This finding was interpreted as impairment in the ability to represent relative value, further supporting a role for the OFC in representing relative reward value (Fellows & Farah, 2005).

Since representing relative reward magnitude is essential for decision-making, it is no large surprise that patients with OFC damage have pervasive decision-making impairments (Elsinger & Damasio, 1985; cf. Wallis, 2007). It appears that these decision-making deficits are not just related to impaired reward-magnitude representation, but also to inflexibility in response strategy. Shifting strategy is a type of exploratory behaviour. For example, if

someone always chooses the same option, they learn nothing about the outcome of other options. To explore their environment, people still occasionally choose alternative options to see what happens, specifically to see if another option is more highly rewarded than the current option. This strategic flexibility has been suggested to be missing in patients with OFC damage (Maia & McClelland, 2004). For example, it has been found that patients with OFC damage fail in a reversal learning paradigm (Rolls, 1994 cf. Rolls, 2004). In this type of paradigm there were two choices, A and B, one of which resulted in reward. Throughout the experiment the reward contingencies were reversed; for example, if selection of choice A resulted in reward, the contingencies would switch so that it was now choice B that resulted in reward. While healthy controls quickly reversed strategies, choosing B over A, it took OFC damaged patients significantly more trials to learn the contingency reversal suggesting that they were not as strategically flexible as the healthy controls (Maia & McClelland, 2004).

A paradox in decision-making theory is that while people still calculate expected reward value as the product of reward magnitude and expected risk, they do not always make the choice that maximises reward value. For example, in a social decision-making game, if a person believes an offer from their partner on how to divide a sum of money between them is unfair, they will refuse the offer resulting in neither partner receiving money. In this instance a person refuses to maximise reward value (no matter how small) so they may punish their partner (Sanfey et al., 2003). The orbitofrontal cortex has been implicated in a similar paradox where minimising regret is chosen over maximising reward (Camille et al., 2004; Coricelli et al., 2007). Healthy and OFC damaged participants were given a choice between different types of gambles; for example, a 20% chance of winning 200Kr, and an 80% chance of losing 50Kr, or a 50% chance of either winning or losing 50Kr. After the trial was completed, participants were shown what would have happened had they chosen one of the other gambles. This allowed them to engage in counterfactual thinking – "if only I had chosen *a* instead of *b*, I would have won *x* instead of losing *y*." Ironically, it was found that while patients with OFC damage behaved according to the mathematical models of decision-making, insofar as they continued to choose gambles which maximised reward value, healthy controls deviated from the models and chose gambles that would minimise regret (Camille et al., 2004). It appears, then, that the OFC, in addition to playing a role in representing relative reward magnitude, may play a role in response-strategy selection.

ANTERIOR INSULAR CORTEX

It has been found that people adjust their decision-making strategy as the risk associated with different decisions changes. This suggests that there is a region of the brain that is able to track risk (Preuschoff et al., 2008; Craig, 2009). The anterior insular cortex (AIC), a region of the brain often activated in decision-making paradigms (Knutson et al., 2000; Sanfey et al., 2003; Knutson et al., 2008; Preuschoff et al., 2008; Clark et al., 2009) is hypothesised to be such a region. It has bidirectional connections with other areas implicated in decision-making like the ventral striatum, OFC, and anterior cingulate cortex (Reynolds & Zahm, 2005) and is activated by ambiguity and uncertainty (Preuschoff et al., 2008). This makes it a good candidate for coding changing risk. It has been suggested that the AIC codes for risk prediction-error in the same manner that the ventral striatum is hypothesised to code for reward prediction-error. According to both Expected Utility Theory (von Neumann & Morgenstern, 1944) and Prospect Theory (Kahneman & Tversky, 1979), people must determine the risk associated with a decision because risk and magnitude are used to calculate expected reward value and it is the option that maximise reward value that should be chosen. If the actual risk is different than the expected risk, a risk prediction-error has occurred. It has been found that bilateral insula activation positively correlates with both expected risk and risk prediction-errors and that these two signals are spatially and temporally separated (Preuschoff et al., 2008). The expected risk signal was found to be located in the dorsal AIC while the risk prediction-error signal is more ventral. Similarly, expected risk elicits AIC activation after a choice has been made and stays active until the choice outcome has been revealed. Conversely, the risk prediction-error signal occurs in a fast on/off manner immediately after choice outcome is known.

While the risk-prediction-error hypothesis satisfies the mathematical component of Prospect Theory and Expected Utility theory, there is an emotional element to decision-making that the theories can not account for and that the AIC may play a part in modulating. It has been suggested that AIC activation may mediate the negative emotion associated with risky decisions and modulate response strategy based on these emotions. To this end, it has been found that insula activation is significantly stronger when choosing the riskier of two options (Paulus et al., 2003b). Similarly, in an ultimatum game where one of two partners determines how a sum of money should be split between the two partners, bilateral AIC activation positively correlates with unfairness of the offer (Sanfey et al., 2003). AIC activation also

positively correlates future rejection of an offer (Sanfey et al., 2003; Knutson et al., 2007), suggesting that it plays a role in response strategy determination as well as tracking risk.

Anterior Cingulate Cortex

In the ultimatum game, activity in the bilateral anterior cingulate cortex (ACC), like the anterior insula**,** positively correlated with unfair trials (Sanfey et al., 2003). The ACC is a region implicated in many different aspects of cognition; it is implicated in attention for target selection, motor response selection, performance monitoring, novelty detection and reward assessment (Bush et al., 2002). The bidirectional connectivity between the ACC, the OFC, anterior insula and ventral striatum (Reynolds & Zahm, 2005) links it to the decision-making network, and many decision-making studies have found that the AIC and ACC are activated together (Craig, 2009). The AIC and ACC are so closely linked, that human imaging studies have found that the ACC, like the AIC, seemed to code risk-prediction error (Brown and Braver, 2005).

Both fMRI and event-related potential studies point to the ACC as involved in some form of error/performance monitoring (Debener et al., 2005; van Veen & Carter, 2006; Taylor et al., 2007). In this body of research, the ACC is implicated in detecting errors that have been committed and interacting with areas of the brain that exert executive control to refocus cognitive resources. This may result in refocusing attentional resources or by affecting a change in strategy. Recent studies have challenged the error/performance monitoring role of ACC demonstrating that it is not activated when errors are predicted or detected, but rather is active when there needs to be a change in behavioural strategy (Bush et al., 2002; Magno et al., 2008). In a human imaging study, dorsal ACC activation has been shown to correlate with the need to switch strategy**,** whether the strategy shift was signalled by a cue or by reduced performance outcome on a task (Bush et al., 2002). More specifically, the dorsal ACC has been shown to be active when a sub-optimal decision-making strategy is employed, whether that strategy is too risky or too conservative (Hewig et al., 2009).

Predicting Future Decisions From Brain Activations

While the majority of fMRI decision-making studies look at brain activation as the end product of a behavioural response, there are several studies that go in the other direction and infer future behaviour from brain activation patterns. It has been found that when deciding whether or not to purchase a product, the stronger the activation in the ventral striatum, the more likely an individual is to subsequently buy the product. Conversely, increased insula and decreased medial prefrontal cortex activity correlated with the subsequent decision to not buy the product (Knutson et al., 2007). Similarly, in a social, decision-making game, increased right anterior insula cortex activity and decreased dorsolateral prefrontal cortex activity correlated with a subsequent rejection of an offer, while the opposite activation pattern resulted in its acceptance (Sanfey et al., 2003). It has also been found that there are neural correlates for individual differences in response strategy. Individuals who showed greater relative activation to monetary losses and gains across the decision-making network were found to be more loss averse and chose more conservative strategies. Those who had relatively weaker activations to gains and losses were less loss averse and chose riskier strategies (Tom et al., 2007). It has also been found that individuals who choose risky decision-making strategies have relatively stronger dorsal ACC activation when they use too cautious a strategy, while cautious deciders show more dorsal ACC activity when they use a decision strategy that is too risky (Hewig et al., 2009).

Present Study

Several studies have suggested that participants use different response strategies when making decisions under risk depending on whether their decisions are rewarded and punished, and to what extent (Elliott et al., 2003; Pessiglione et al., 2006; Cooper & Knutson, 2008). Others have shown that individual differences in response strategy correlate with different neural sensitivities in the ventral striatum, insula and anterior cingulate cortex (Tom et al., 2007; Hewig et al., 2009). These studies, however, were not primarily investigating differences in response strategy and their findings to that effect were coincidental. Since strategic differences within and between experiments using different financial contingencies may confound decision-making findings, the present study seeks to investigate whether strategic differences do indeed exist, and what impact they may have on BOLD fMRI activation.

In the present study, we will use signal detection theory to investigate how both a monetary reward and a monetary punishment response contingency affect decision-making strategy on a continuous performance task and whether differences can be localised to the ventral striatum, anterior cingulate cortex, orbitofrontal cortex, and anterior insular cortex - four regions of interest implicated in reward and decision-making as described above.

HYPOTHESIS

Reward and Punishment Contingencies vs. No Reward Contingencies

Since it is theorised that the ventral striatum, orbitofrontal cortex and anterior insular cortex respectively represent expected reward value, reward magnitude and expected risk, these brain regions will show more activation when responding under both the reward and the punishment contingencies than when responding without monetary reward or penalty. Since the anterior cingulate is implicated in strategy shifting and in performance monitoring, there will be stronger activation in this region when there is a monetary contingency and failure to properly monitor performance and switch strategy results in financial loss. Monetary contingency will not affect the ability to detect a target from amongst distracters. However, since it has been found that post-error slowing occurs after infrequent errors and post-correct slowing occurs after infrequent correct trials (Notebaert et al., 2009), response time will be slower for the reward and punishment contingencies where task performance is emphasised by financial gain and loss than for the no monetary contingency where no performance feedback is given. In line with findings from Cooper and Knutson (2008), response bias will be more liberal when there are monetary consequences than when there are no monetary consequences.

Reward vs. Punishment

It has been found that people are loss averse and will only accept a gamble if the amount that can be won is twice as large as the amount that can be lost (Kahneman & Tversky, 1979). It has been proposed that this phenomenon can be explained by neuroimaging data that found that in several decision-making areas, including the ventral striatum, anterior cingulate cortex, and orbitofrontal cortex, losses are associated with stronger activations than gains (Tom et al., 2007). With this finding in mind we hypothesise that activation in the four regions of interest

will be greater, response time will be slower, and response strategy will be more conservative for punishment than for reward.

METHODS

ETHICS

This study was approved by the regional committee for medicine and health research South-East A (REK Sør-Øst A). Protocol number S-08549a.

PARTICIPANTS

Eighteen participants (mean age ± SD = 24.8 ± 1.9years; 7 females) were recruited for the study in accordance with regional ethics committee guidelines and provided written informed consent. All subjects were free of neurological, psychiatric and substance abuse problems. They did not have a history of problem gambling, medical problems, nor were they undergoing any medical treatment that could affect cerebral blood metabolism and blood flow. Subjects were paid 300 Kr for their participation (150Kr for the screening interview and 150Kr for participating in the experimental paradigm) and kept any additional money they won in the task described below.

DESIGN & DATA ACQUISITION

Experimental Paradigm

The paradigm was created and run in E-Prime software (version 1.2; Psychology Software Tools, Inc.; Pittsburgh, PA, USA). Stimuli were presented to the participants in the scanner using NNL's VisualSystem (NordicNeuroLab, Bergen, Norway) and responses were collected using NNL's ResponseGrips (NordicNeuroLab, Bergen, Norway).

Monetary contingency (Reward, Punishment and No contingency) was manipulated with a within-subject block design using a modified continuous performance task divided into two 8.5 minute sessions. The first session (Reward) consisted of three continuous performance tasks (CPTs) organised into blocks. The three tasks were a baseline arrow task (BASE), a modified CPT signal-detection task where 3Kr was won for correct responses while 1Kr was lost for incorrect responses (REW), and the same modified CPT without a reward contingency (NC-REW) (Table 1). The sequence of blocks was fixed with the baseline arrow block always preceding each of the continuous performance blocks (Fig. 1). Both of the CPT

blocks were 28s long and were each repeated six times per session. The baseline arrow block was repeated twelve times per session, and was only 14s in duration so participants spent the same total amount of time on each block type.

The second session (Punishment) was identical to the first except the reward contingencies were reversed in the block with a monetary contingency (PUN) – 1Kr was won for correct responses and 3Kr was lost for incorrect responses. The no contingency CPT block in this session is referred to as "NC-PUN". In both sessions, non-responses in the CPT blocks were penalised 3KR. Response handedness, task background colour, and session order were counter-balanced over subjects.

Table 1. Abbreviations used for the different block types across sessions.

	Baseline	**Monetary Contingency**	**No Monetary Contingency**
Reward Session	BASE	REW	NC-REW
Punishment Session	BASE	PUN	NC-PUN

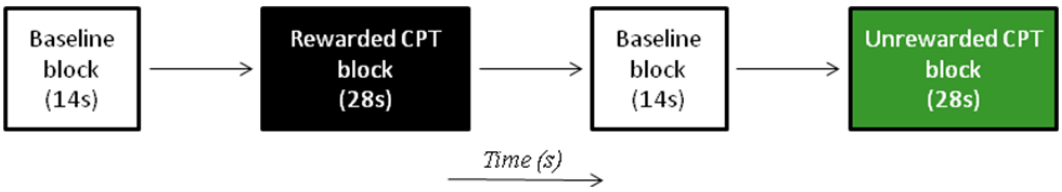

Fig. 1. The sequence of blocks within the reward session. This sequence is repeated six times resulting in twelve presentations of the Baseline block and six presentations each of the Rewarded and Unrewarded CPT blocks. The sequence is the same in the punishment session.

Individual trials on each of the three CPT blocks were composed of an identical series of events. A stimulus was presented for 300ms followed by a response screen for 1300ms. Participants could respond during either of these two screens. Once a response was made a feedback screen was presented for 750ms after which the next stimulus appeared (Figs. 2, 3 &

4). What differed between the three tasks were the stimulus presented, and the feedback given.

In the BASE block, six left or six right facing arrows were presented (Fig. 2). Participants were instructed to press the corresponding button i.e. press the left button for the left-facing arrows. If the participant's response was correct, they would see the word *"Correct"* in black letters during the feedback screen. If their response was incorrect, the word "Incorrect" in red letters was presented.

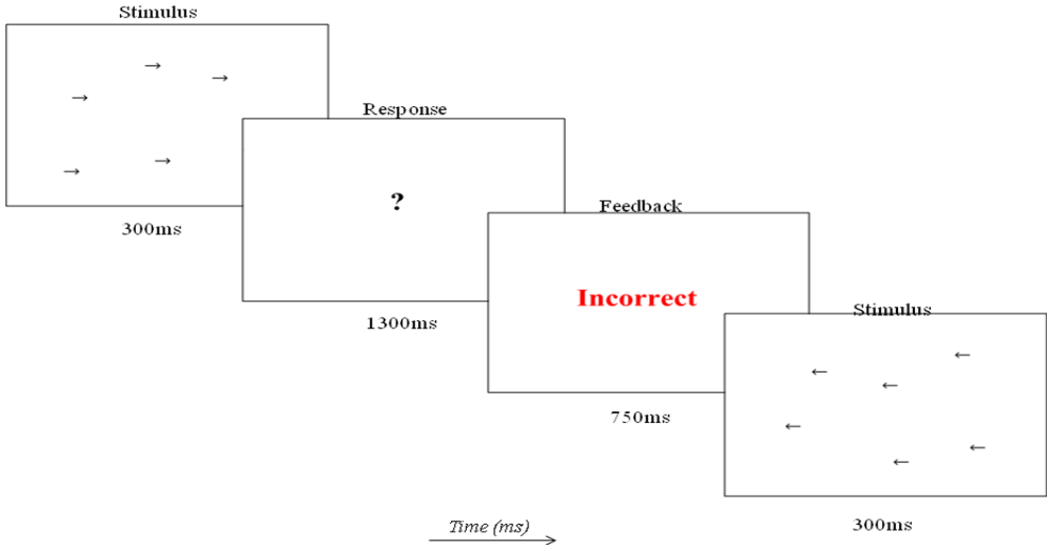

Fig. 2. Baseline block. Participants must indicate the direction the arrows are facing with a corresponding left or right button press. They can respond during either the stimulus or the response screen. Feedback is given; however, there are no monetary consequences.

The stimuli for the CPT blocks were black and white line drawings of various objects (Snodgrass & Vanderwart, 1980). The participants' task was to determine whether one of the six pictures displayed depicted an animal or an insect – the target stimulus. They responded with a button-press when the target was present and with a button-press using the other hand when the target was absent. Different background colours were used to indicate whether there was a reward contingency in the ongoing block. When the background of the screens was black, the win and loss of money was contingent on performance (Fig. 3). During the feedback screen**,** participants saw their total winnings fluctuate up and down as they responded correctly and incorrectly. When the screens' background was green, the task was the same, however, there was no reward contingency (Fig. 4). Regardless of the veracity of

the answer**,** the amount won stayed constant. This was indicated during the feedback screen where the same amount (what had been won so far) was always displayed after each trial.

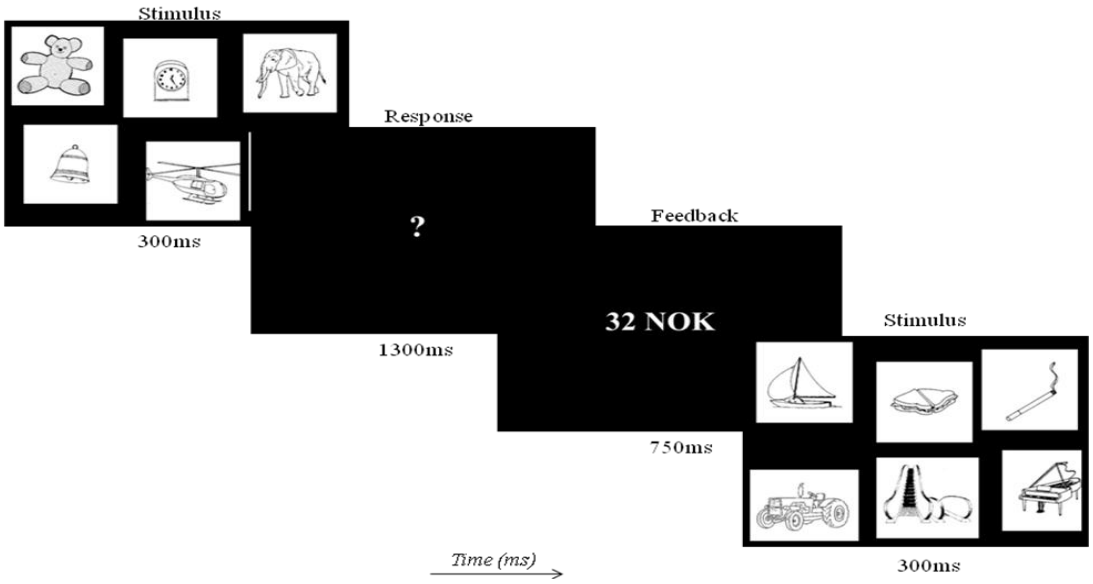

Fig. 3. Reward & Punishment blocks. The stimulus is presented for 300ms followed by a question mark for 1300ms. Participants may respond during either of these two screens at which point the feedback screen depicting the total amount of money won is immediately presented. The next trial begins after the feedback screen.

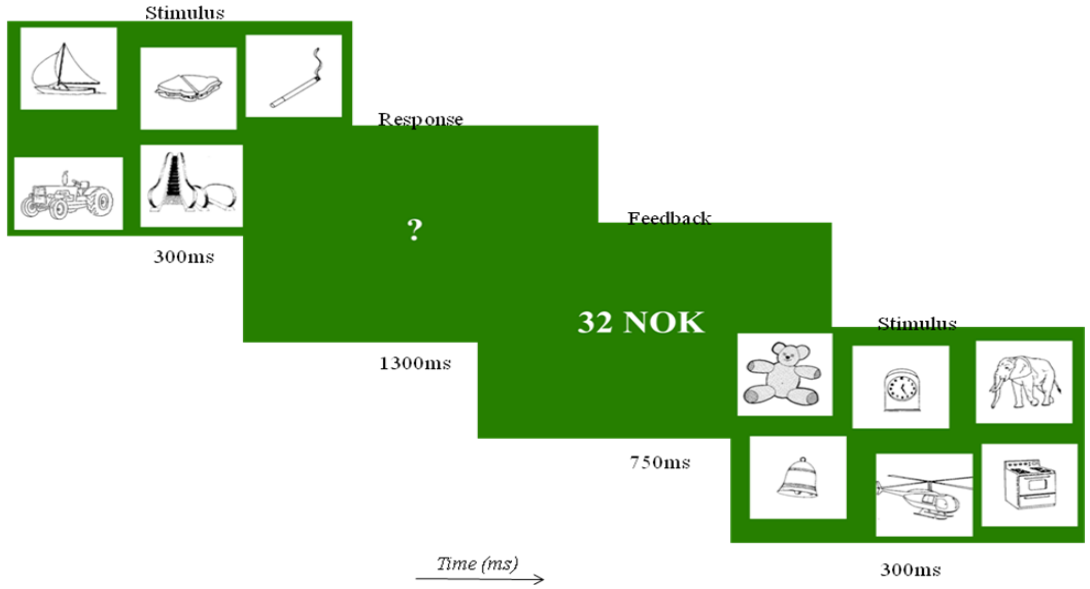

Fig. 4. The No Contingency block is identical to both the Reward and Punishment blocks except there are no monetary consequences, no feedback given and the background colour is different. The money won so far was displayed during the feedback screen and remained unchanged through the duration of this block.

Procedure

Participants were recruited using a poster approved by the regional ethics committee (Appendix A). The poster indicated that we were conducting an fMRI study and that participants would be paid for their time. An e-mail address was provided for those who were interested in receiving further information. Those who replied received an e-mail indicating that their participation would be needed over two days – one day to complete an hour long, in-person interview, and the other day for scanning. Those who still expressed an interest were contacted by telephone and asked general questions about their somatic and mental health as well as their suitability for participation in an fMRI study. The experience of lying in a scanner, viewing a screen through goggles and responding using response grips was described to the participants. Those who were not excluded and were still interested in participating were booked for an in-person interview.

At the outset of the in-person interview, the experimental paradigm (a more basic description of the paradigm below) was described to the participant and informed consent was given. The MINI International Neuropsychiatric interview (Norwegian version 5.0.0) based on DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) criteria was used to assess mental health. Participants were also screened to ensure there was nothing that could preclude them from participation (e.g. they were pregnant or had claustrophobia).

A Norwegian version of the DSM-IV Pathological Gambling Diagnostic Form was used to assess problem gambling.

As part of the screening interview participants completed a short, practice version of the paradigm to ensure that they were capable of performing the task. By completing a practice version, a confounding learning effect would be reduced if not eliminated (Knutson et al., 2001a). In the practice version, pictures depicting modes of transportation were used as target stimuli. These pictures were removed from the experimental task to avoid potential confusion.

On the scanning day, participants entered the scanner and were oriented to the goggles and response grips. The initial localiser scan was followed by the structural acquisition which was followed by the experimental paradigm described below.

fMRI Data Acquisition

Imaging was conducted at Oslo University Hospital - Ullevål using a General Electric Signa HDx 3T scanner with a standard eight channel head coil (General Electric Company; Milwaukee, WI, USA). Cushions were placed around the participants' heads to prevent motion and earplugs were used to minimise noise.

An axial localizer scan was used to orient all subsequent scans and a high-resolution, anatomical image was acquired using a T_1-weighted GE FSPGR Bravo sequence (TR = 10.9s; TE = 4.6s; FA = 13°: 248 axial slices; 1.2mm thick; 240 mm x 240mm in-plane resolution, 352x224 matrix) prior to functional imaging. Functional images were acquired with a T_2*-weighted, echo-planar imaging sequence sensitive to the BOLD contrast (TR = 2s; TE = 25ms; FA = 90°). 263 volumes were acquired in each session, the first eight of which were dummy volumes used to ensure that there was homologous tissue magnetisation. Each volume consisted of 36 slices acquired parallel to the AC-PC plane (sequential acquisition; 3.5mm thick with a 0.5mm gap; 260mm x 260mm in-plane resolution, 64 x 64 matrix).

Data Quality

The images were visually inspected for artefacts, abnormal variance and for signal dropout due to magnetic susceptibility in the region of the ventral striatum and the orbital frontal cortex. One participant was excluded from analysis because she revealed post-scanning that she didn't realise she would receive actual money.

DATA ANALYSIS

Behavioural Analysis

Behavioural analyses were performed with SPSS 16.0 for Windows (Microsoft Corporation; Redmond, WA, USA). Significant differences were identified at $p < 0.05$ using paired-sample *t*-tests, testing for the main effect of reward contingency on response time, response bias ($\ln\beta$), and signal detection (d').

Signal detection theory (SDT) measures how well participants are able to detect signal from noise and how liberally or conservatively they say a signal is present. SDT makes the assumption that there are two overlapping Gaussian distributions (Green and Swets, 1966 &

MacMillan and Creelamn, 2001). One distribution is noise alone, and the other is signal + noise (Figure 5). The larger the distance between the peaks, the easier it is to discriminate signal from noise. Discriminability can be determined using SDT by measuring the distance between the peaks of the distributions - a measure known as d'. How liberally or conservatively a participant says, "yes a signal is present" is known as the criterion value or response bias. SDT is used to calculate this value giving an indication of the strategy employed by the participant in determining signal from noise.

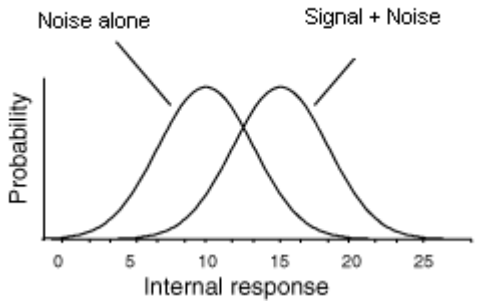

Fig. 5. Noise and signal + noise distributions.

On each trial in a standard yes-no paradigm a signal is either present or absent. Four types of responses can result: a hit, the participant correctly identifies that a signal is present; a miss, the participant incorrectly indicates that a signal is absent when in fact, it is present; a correct negative, the participant correctly identifies that there is no signal; and a false positive, the participant indicates that a signal is present when it is not (Table 2).

Table 2. The four possible response types on a binary decision-making task.

		Signal	
		Present	Absent
Response	"present"	*Hit*	*False Positive*
	"absent"	*Miss*	*Correct Negative*

Two important pieces of information are garnered from this table – the hit rate (HR) and the false positive rate (FPR). The HR is calculated as the proportion of hits when a signal is present, and the FPR is calculated as the proportion of false positives on noise alone trials. Using these values we can calculate discriminability:

$$d' = Z(HR) - Z(FPR)$$

where Z(HR) and Z(FPR) are transformations of the hit and false positive rates to inverse Z-scores,

and response bias:

$$\ln\beta = -0.5 * d' * [Z(HR) + Z(FPR)]$$

as used in Tsoi et al. (2008), Mashal and Faust (2008), and Macmillan and Creelman (1990). When there is no sensitivity (i.e. the participant cannot discriminate signal from noise), d' = 0. When a response is unbiased, lnβ = 1. A lnβ-value > 1, indicates that a participant has a conservative response bias and tends to prefer to say, "No, a signal is not present." Conversely, a lnβ < 1 indicates the participant has a liberal response bias and tends to say, "Yes, a signal is present."

Image Analysis

All images were converted from dicom to NIfTI image format using nordicICE (version 2.2.9; NordicImagingLab AS; Bergen, Norway). Image analysis was conducted using Statistical Parametric Mapping (SPM5, http://www.fil.ion.ucl.ac.uk/spm/spm5/; Wellcome Trust Centre

for Neuroimaging, London, UK). All volumes were realigned to the first volume (Friston et al., 1995a) and the anatomical image was co-registered to the mean functional image to ensure that they were aligned. Each subject's structural image was spatially normalised to the Montreal Neurological Institute (MNI) T_1-weighted template image supplied with SPM5 (Friston et al., 1995b). The functional images were then spatially normalised using the parameters obtained in the structural normalization, resampled to a voxel size of 3x3x3mm, and smoothed using an 8mm full-width at half-maximum Gaussian kernel. A high-pass-filter using a cut-off value of 128s was applied to compensate for signal drift, and the default SPM5 low pass filter was applied to reduce the effects of physiological noise.

A boxcar model convolved with a synthetic hemodynamic response function was used (Friston et al., 1995a). Three contrasts were tested for significance using a two-stage, random-effects, ROI analysis. The REW and NC-REW blocks were contrasted; the PUN and NC-PUN blocks were contrasted; and the REW and PUN blocks were contrasted. In the first stage of this analysis, contrast images for each subject, for each contrast of interest were created. The single-subject contrast images were then included in a second-level, random-effects analysis. This analysis was performed for each of the three contrasts of interest. To test the a priori hypotheses we had about signal changes in the bilateral ventral striatum, anterior cingulate cortex, insula and orbitofrontal cortex, small volume corrections based on anatomically predefined ROIs using the SPM WFU PickAtlas toolbox (version 2.3, http://fmri.wfubmc.edu/cms/software#PickAtlas; Wake Forest University School of Medicine; Maldjian et al., 2003 & Maldjian et al., 2004) were applied.

Correlation Analyses

A voxelwise correlation between change in response bias ($\Delta \ln \beta$) and contrast images [PUN-(NC-Pun)] was performed.

RESULTS

BEHAVIOURAL RESULTS

Paired-sample *t*-tests indicated that there was not a significant difference in response time for any of the four response outcomes (hit, miss, correct negative, and false positive) or the ability to detect signal from noise (*d-prime*) between the reward and no-reward contingency (REW vs. NC-REW) (Table 3a); the punishment and the no punishment contingency (PUN vs. NC-PUN) (Table 3b), or between the reward and punishment contingency (REW vs. PUN) (Table 3c). In the PUN vs. NC-PUN comparison, there was a significant difference in response bias, $t = -4.11$, $p < 0.001$. This indicated that participants adopted a more liberal response strategy, i.e. they were more likely to say a target was present when their incorrect responses were punished than when no monetary contingency was associated with their responses (Table 3b).

Table 3a. Reward vs. No Reward

	REW	***NC-REW***	***t***	***p***
Response Time (ms)	718 ± 144	722 ± 145	-0.37	n.s.
d-prime (d´)	1.89 ± 0.68	1.78 ± 0.74	1.14	n.s.
Response Bias (lnß)	0.22 ± 0.65	0.44 ± 0.85	-1.55	n.s.

Table 3b. Punishment vs. No Punishment

	PUN	***NC-PUN***	***t***	***p***
Response Time (ms)	731 ± 123	726 ± 126	0.25	n.s.
d-prime (d´)	1.73 ± 0.68	1.75 ± 0.69	-0.15	n.s.
Response Bias (lnß)	0.13 ± 0.64	0.50 ± 0.67	-4.11	0.001*

Table 3c. Reward vs. Punishment

	REW	***PUN***	***t***	***p***
Response Time (ms)	718 ± 144	731 ± 123	-0.35	n.s.
d-prime (d´)	1.89 ± 0.68	1.73 ± 0.68	0.94	n.s.
Response Bias (lnß)	0.22 ± 0.65	0.13 ± 0.64	0.62	n.s.

Values are reported as mean ± standard deviation. Reported *p* values reflect the results of paired sample *t*-tests.

IMAGING RESULTS

Reward vs. No Reward

Significant activations were found in the bilateral: ventral striatum, anterior cingulate cortex, anterior insula, ventral lateral OFC, and the right dorsal lateral OFC when responding for reward (REW) compared to responding without a reward contingency (NC-REW) (Table 4 & Figs. 6 & 7). In addition to the a-priori defined regions of interests, a whole brain analysis ($p < 0.05$, FDR corrected; extent cluster k > 25 voxels) found one significant cluster in the right lingual gyrus (MNI coordinates: x, y, z = 39, -81, -18; $z = 6.85$; $p < 0.001$).

Table 4.
REW vs. NC-REW: fMRI ROI results

ROI	*Laterality*	*x*	*y*	*z*	*Peak z-score*	*p(FDR-corr)*
Ventral striatum	right	15	12	-6	4.82	< 0.001
	left	-12	9	-6	4.03	< 0.001
Anterior cingulate cortex	right	15	33	27	4.70	< 0.001
	left	-3	33	27	3.26	< 0.01
Anterior insula	right	33	21	-6	5.02	< 0.001
	left	-30	21	-12	4.43	< 0.001
Ventral lateral OFC	right	24	48	-18	5.67	< 0.001
	left	-30	18	-12	4.38	< 0.001
Dorsal lateral OFC	right	45	42	15	3.78	< 0.005

Data are thresholded at $p < 0.05$ (*FDR*-corrected) and only clusters with > 25 voxels are reported. ROI anatomical region, hemisphere and coordinates are based on the Montreal Neurological Institute (MNI) system.

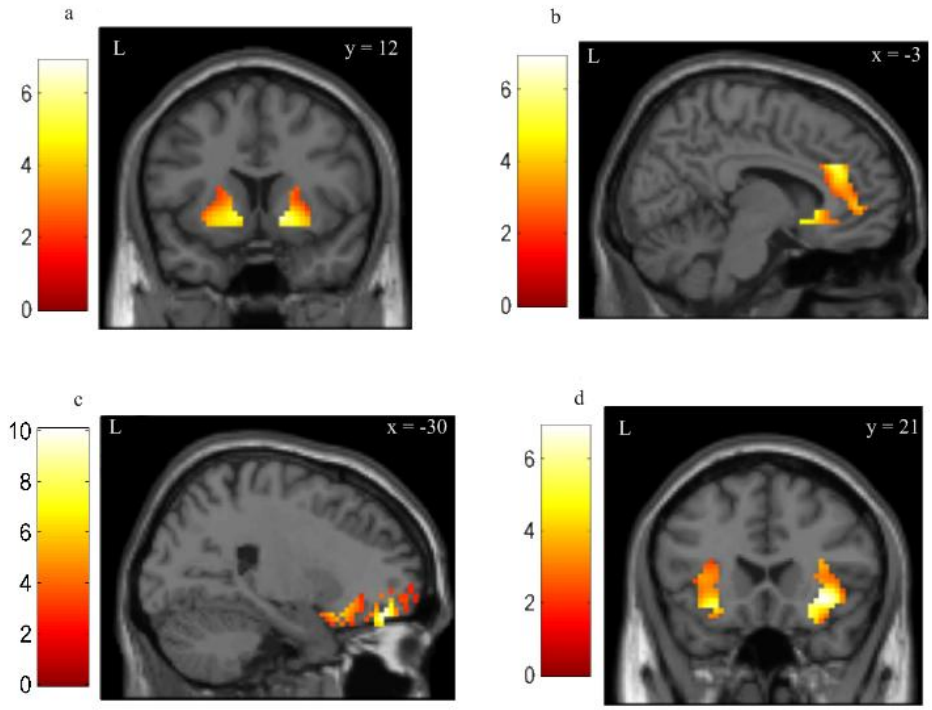

Figure 6. Differences in BOLD fMRI activations between the REW block and the NC-REW block: (a) ventral striatum; (b) anterior cingulate cortex; (c) orbitofrontal cortex; (d) anterior insula. Colours refer to t-values.

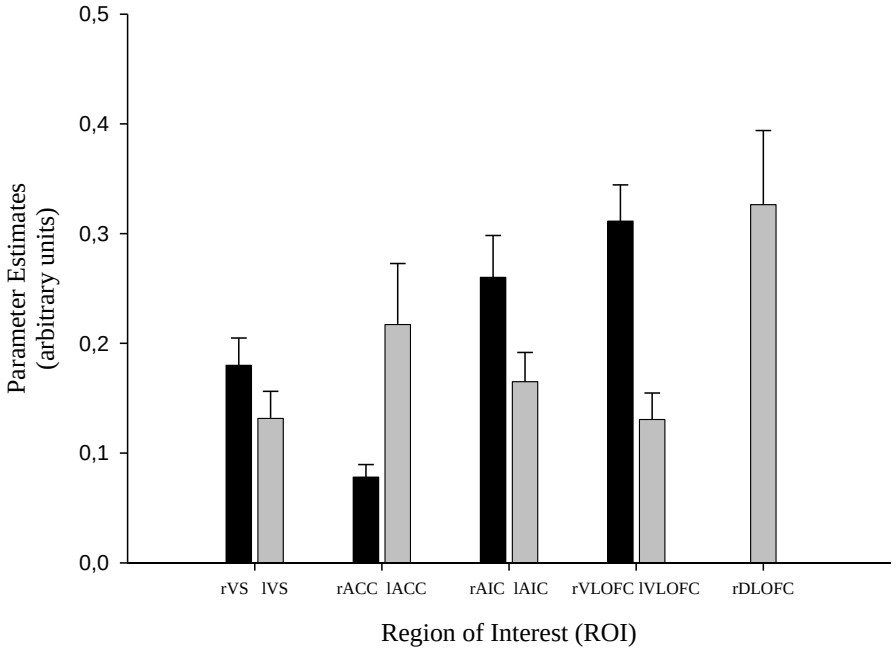

Figure 7. Parameter estimates ± S.E.M. indicating greater activation in the REW than in the NC-REW block: rVS = right ventral striatum; rACC = right anterior cingulate cortex; rAIC = right anterior insula cortex; rVLOFC = right ventrolateral orbitofrontal cortex; rDLOFC = right dorsolateral orbitofrontal cortex.

Punishment vs. No Reward

Significant activations were found bilaterally in the: ventral striatum, anterior insula, ventral lateral OFC and in the right anterior cingulate cortex and dorsal lateral OFC when responding under the punishment contingency (PUN) compared to responding without a monetary punishment contingency (NC-PUN) (Table 5 & Figs. 8 & 9). A whole brain analysis ($p < 0.05$, *FDR*-corrected; extent cluster k > 25 voxels) was conducted and no areas outside of the ROIs survived error correction.

Table 5.

PUN vs. NC-PUN: fMRI ROI results

ROI	*Laterality*	*x*	*y*	*z*	*Peak z-score*	*p(FDR-corr)*
Ventral striatum	right	15	9	-9	4.03	< 0.01
	left	-12	12	-6	2.88	< 0.05
Anterior cingulate cortex	right	12	36	27	3.26	< 0.05
Anterior insula	right	30	15	-12	4.21	< 0.005
	left	-30	24	-6	3.83	< 0.005
Ventral lateral OFC	right	21	48	-21	3.91	< 0.01
	left	-24	48	-18	3.24	< 0.05
Dorsal lateral OFC	right	42	51	18	4.12	< 0.05

Data are thresholded at $p < 0.05$ (*FDR*-corrected) and only clusters with > 25 voxels are reported. ROI anatomical region, hemisphere and coordinates are based on the Montreal Neurological Institute (MNI) system.

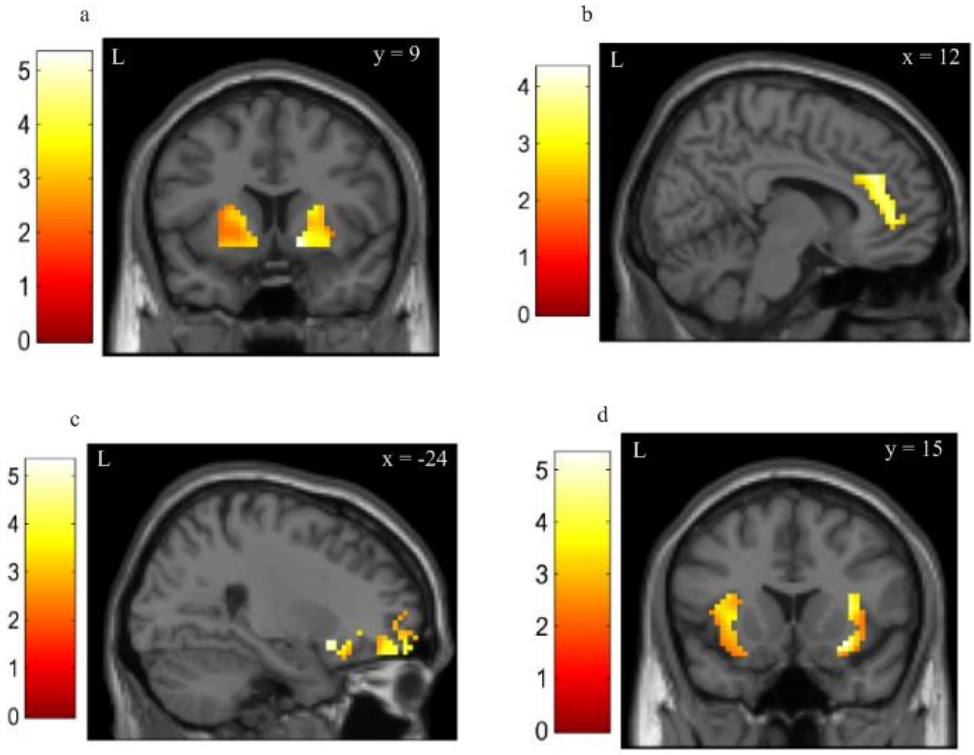

Figure 8. Differences in BOLD fMRI activation between the PUN and NC-PUN blocks: (a) ventral striatum; (b) anterior cingulate cortex; (c) orbitofrontal cortex; (d) anterior insula. Colours refer to t-values.

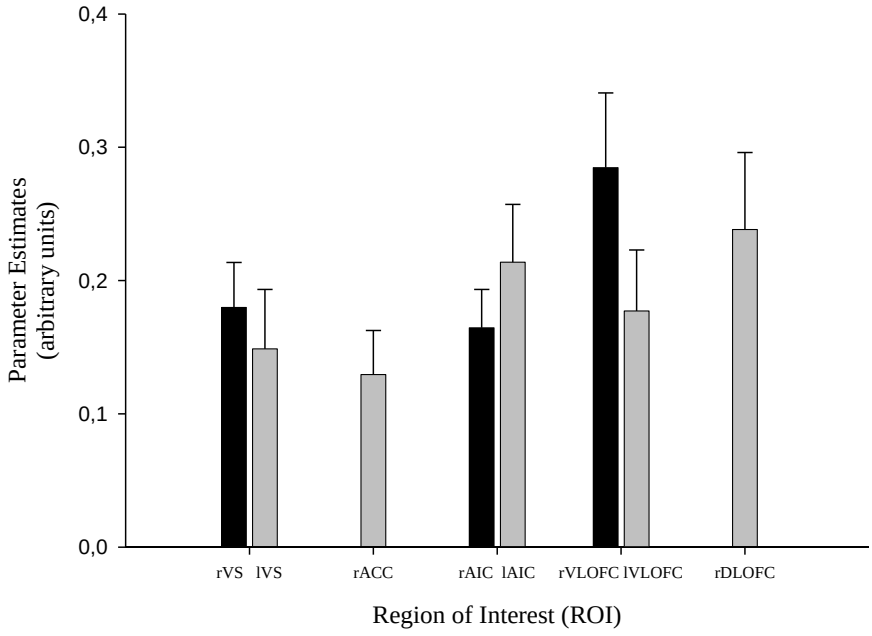

Figure 9. Parameter estimates ± S.E.M indicating greater activation in the PUN than in the NC-PUN block: rVS = right ventral striatum; rACC = right anterior cingulate cortex; rAIC = right anterior insula cortex; rVLOFC = right ventrolateral orbitofrontal cortex; rDLOFC = right dorsolateral orbitofrontal cortex.

Reward vs. Punishment

There were no significant activations in the four predefined ROIs when contrasting the reward contingency (REW) with the punishment contingency (PUN). A whole brain analysis was conducted, ($p < 0.05$, FDR corrected; extent cluster k > 25 voxels) and no areas outside of the ROIs survived error correction.

CORRELATIONS

To examine the significant difference in response strategy between the Punishment (PUN) and No Punishment Contingency (NC-PUN) blocks, correlation analyses using response strategy (lnβ) and BOLD fMRI activation were modelled in SPM5. Positive correlations between change in response strategy (Δlnβ) and BOLD fMRI activation were found in the bilateral dorsolateral prefrontal cortex (DLPFC), the right supplementary motor area (SMA), the right middle temporal gyrus, and the right ventral lateral OFC (Table 6 & Fig. 10). A negative correlation was found between change in response strategy and the right cerebellum, and the right medial ventral OFC (Table 7 & Fig. 11)

Table 6.

Positive correlations between change of strategy and BOLD signal

ROI	*Laterality*	*x*	*y*	*z*	*r*	*p(uncorrected)*
DLPFC	right	33	15	30	0.71	< 0.001
	left	-51	36	15	0.77	< 0.001
SMA	right	12	-6	75	0.7	< 0.001
Middle Temporal Gyrus	right	54	-75	21	0.67	< 0.005
Ventral lateral OFC	right	27	63	-3	0.64	< 0.005

Data are thresholded at $p < 0.01$ (uncorrected) and only clusters with > 25 voxels are reported. ROI anatomical region, hemisphere and coordinates are based on the Montreal Neurological Institute (MNI) system. DLPFC = dorsolateral prefrontal cortex; SMA = supplementary motor area; OFC = orbitofrontal cortex.

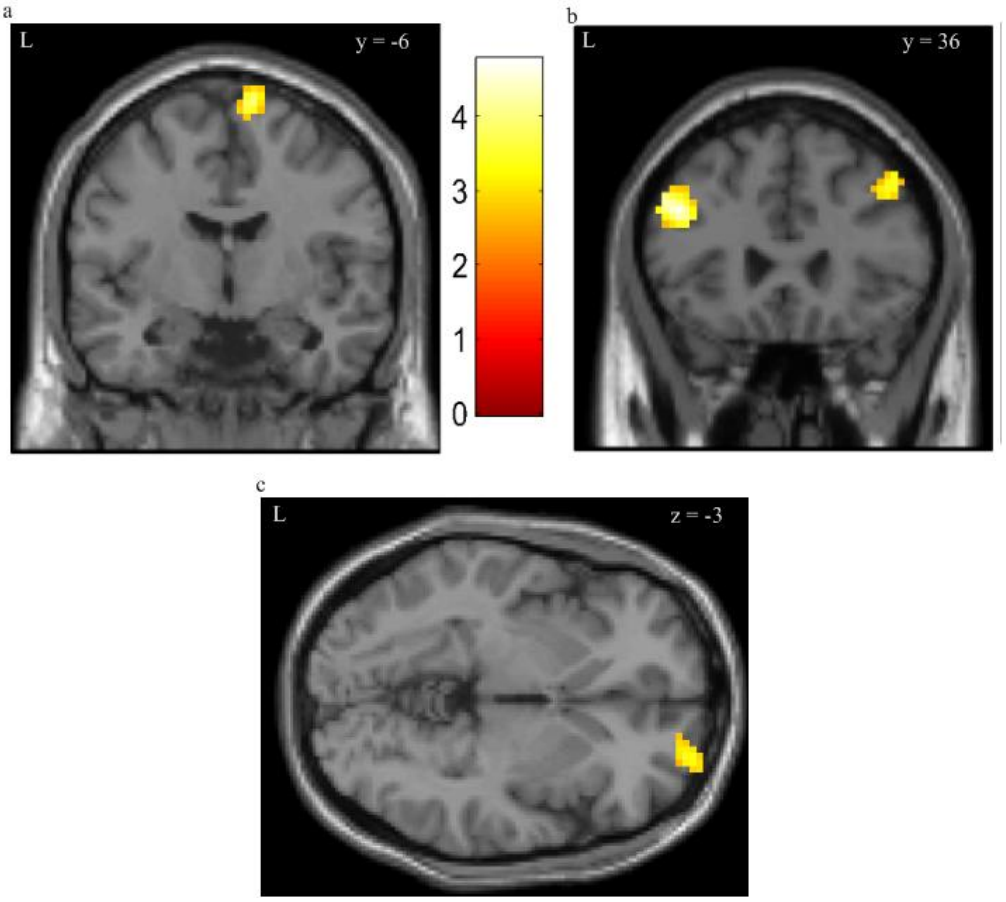

Figure 10. Positive correlations between BOLD fMRI activation and change in response strategy (Δlnβ): (a) right Supplementary Motor Area; (b) bilateral DLPFC; (c) right ventral lateral OFC. Colours refer to t-values.

Table 7.

Negative correlations between change of strategy and BOLD signal

ROI	*Laterality*	*x*	*y*	*z*	*r*	*p(uncorrected)*
Cerebellum	right	21	-84	-45	-0.7	< 0.001
Medial ventral OFC	right	6	69	-18	-0.62	< 0.005

Data are thresholded at $p < 0.01$ (uncorrected) and only clusters with > 25 voxels are reported. ROI anatomical region, hemisphere and coordinates are based on the Montreal Neurological Institute (MNI) system. OFC = orbitofrontal cortex.

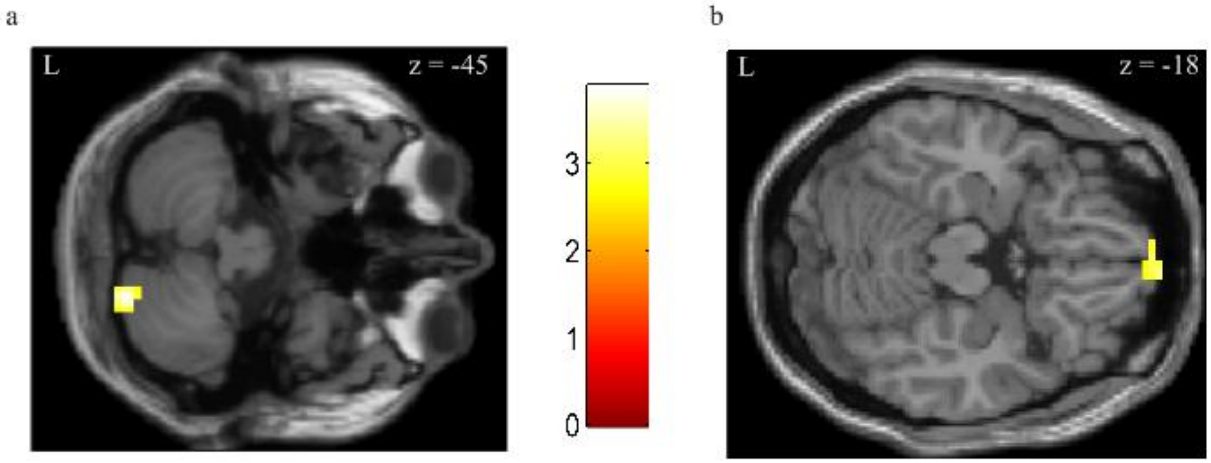

Figure 11. Negative correlations between BOLD fMRI activation and change in response strategy: (a) right cerebellum; (b) right medial ventral OFC. Colours refer to t-values.

DISCUSSION

SUMMARY OF FINDINGS

This study replicates earlier studies showing that when financial reward or punishment is contingent on the outcome of a decision, four regions implicated in financial decision-making, the ventral striatum, orbitofrontal cortex, anterior insula and anterior cingulate cortex, are activated. This study also finds that a more liberal response bias is adopted when responding to avoid punishment than when responding without financial contingency, and that greater strategic flexibility correlates with: success on the task; increased activation in the bilateral dorsolateral prefrontal cortex, right: supplementary motor area, middle temporal gyrus and ventral lateral OFC; and with decreased activation in the right cerebellum and ventral medial OFC.

The present study was conducted because previous functional MRI studies suggested that people may employ different response strategies depending on whether a financial reward or punishment is contingent on their decision. By using a block design and signal-detection measures, we were able to isolate the strategic differences. However, using this type of design limited how our reward-related activations could be interpreted. Typical functional MRI studies investigating financial decision-making use an event-related design. Since event-related designs better elucidate the time course of the decision-making process, the emphasis of the current literature has been on distinguishing the different temporal components of decision-making. For example, event-related designs have facilitated imaging the differences in activation between anticipating a reward and receiving a reward (Knutson et al., 2001a; Knutson et al., 2001b). With the block design currently employed, these temporal differences cannot be distinguished, that is, we are unable to separate activations related to reward anticipation and outcome, nor are we able to separate activations between loss trials and gain trials. A block design, however, is more robust and is a better tool for investigating strategic differences – the primary goal of this study.

We know from the neuroeconomic perspective that the brain needs to compute the magnitude of the outcome and the risk associated with a particular decision – how big it is, and how likely it will be obtained (Rolls, 2000; O'Doherty, et al., 2001; Knutson et al., 2003; Paulus et al., 2003b; Elliott et al., 2008; Preuschoff et al., 2008; Craig, 2009). It also needs to track the disparity between the expected value of a decision and the realised value of the decision to

calculate prediction-error (McClure et al., 2003; Pessiglione et al., 2006; Seymour et al., 2007; Hare at al., 2008). Current functional MRI and animal literature suggests that each of these decision-making components: magnitude, risk, value, and error-prediction involve the orbitofrontal cortex, anterior insular cortex and the ventral striatum respectively (Rolls, 2000; O'Doherty, et al., 2001; Knutson et al., 2003; McClure et al., 2003; Paulus et al., 2003b; Pessiglione et al., 2006; Seymour et al., 2007; Elliott et al., 2008; Hare at al., 2008; Preuschoff et al., 2008; Craig, 2009). Since the task used in the present study has all the elements needed to measure financial decision-making under risk – a binary choice, uncertain outcome, and different amounts of money won and lost – and it activates a neural-network reliably activated in other financial decision-making studies, it can be concluded that the present approach is a valid measure of financial decision-making. As such, the findings regarding strategic shifts should be applicable to studies using event-related design.

STRATEGY SHIFT

Since previous decision-making literature suggested that different magnitudes of financial reward and punishment seemed to influence response strategy, we hypothesised that a different response strategy would be used from a predominantly rewarded to an unrewarded contingency and from a predominantly punished to an unpunished contingency. Contrary to this hypothesis, a strategic difference was only found for the punishment contingency. According to Prospect Theory people are more sensitive to potential losses than to potential gains. For example, in a 50/50 gamble the amount to be won has to be double the amount to be risked before people will accept the gamble (Kahneman & Tversky, 1979). There appears to be a neural correlate to this disparity in sensitivity. Functional MRI studies have demonstrated that the BOLD response in the ventral striatum, orbitofrontal cortex, anterior cingulate and the ventral lateral and medial prefrontal cortex is greater for losses than for gains of the same magnitude (Tom et al., 2007). It is possible then, that a strategic shift was not observed for the reward contingency in the present study because the reward magnitude used was not large enough.

The response strategy shift that occurred in the punishment contingency was from a fairly liberal response bias (more likely to say "yes" a stimulus was present) on the non-contingent task, to an even more liberal response bias on the punishment contingency task. While the present study did not find a strategy shift driven difference in activation, recent imaging literature has implicated reward-related regions. It has been found that response bias becomes

more liberal with age and that this shift is possibly due to age-related changes in the frontal cortex (Windmann et al., 2002; Huh et al., 2006). Supporting this theory is the finding that patients with dorsal lateral prefrontal cortex lesions use a more liberal response bias than healthy controls in a recognition memory test (Swick & Knight, 1999) and the finding that amnesic patients with anterior limbic system damage, including the OFC, end-up using a more liberal response bias because they cannot suppress false positive responses (Schnider & Ptak, 1999). These findings suggest that the frontal cortex, and possibly the OFC, plays a role in determining response strategy. It is, therefore, possible that some of these same regions played a role in the strategic differences observed in the present study, but were not as easily observed as in patients whose strategic differences are lesion-related.

STRATEGIC FLEXIBILITY

Strategic flexibility is an important component of behaviour. We make decisions based on information we receive from our environment about the risk and magnitude of certain options. However, once we have made a choice, and persist in that choice, we learn nothing new about the environment. This is why a rewarded choice is occasionally abandoned in favour of exploring other options (Rolls, 2004). Exploring alternatives allows one to update the information one has about their environment. According to Shannon (1948), the more uncertain the outcome, the more information the outcome contains (Shannon, 1948 cf. Dreher et al., 2006). In the present study, greater strategic flexibility was associated with better performance during the punishment contingency and was correlated with increased ventral lateral orbitofrontal cortex activations and decreased ventral medial OFC activation. Previous studies have found that lateral OFC activation correlates with punishment magnitude while medial OFC activation correlates with reward magnitude (O'Doherty et al., 2001). In keeping with the present results, it has also been reported that as activation in the lateral OFC increases, activation in the medial OFC decreases (O'Doherty et al., 2001). Since there is a greater neural sensitivity to losses than gains, and individuals who exhibit relatively greater activation in the OFC are more loss averse (Tom et al., 2007), it is possible that a heightened sensitivity to loss aversion is driving strategic flexibility. Greater flexibility, then, may allow for greater avoidance of loss.

Another region that correlated with strategic flexibility was the dorsolateral prefrontal cortex. The DLPFC is considered to be a centre of executive function involved in directing attention, suppressing irrelevant stimuli, retrieving relevant memories and in planning behaviour

(Moghaddam & Homayoun, 2008). In decision-making paradigms it has been found to be active when determining whether or not to act regardless of whether an action is subsequently undertaken (Kühn & Brass, 2009; Karch et al., 2009). For example, in a go/no-go paradigm, the DLPFC was active when determining whether or not to respond to a stimulus (Karch et al., 2009). It is possible then, that heightened loss sensitivity results in increased DLPFC activation, which in turn acts to exert more efficient control over attention, memory, stimulus suppression and behavioural planning, allowing for better avoidance of punishment. However, there is an alternative explanation. One of the tenets of Prospect Theory is that we overweight small probabilities and underweight large probabilities (Kahneman & Tversky, 1979). It has been found that increased activation in the DLPFC is correlated with overweighting a probability, while decreased activation in the same area is correlated with underweighting large probabilities (Tobler et al., 2008). The increased DLPFC activation correlated with strategic flexibility may be related to greater overweighting of the loss. Overweighting the loss may in turn be what is driving the underlying greater sensitivity to loss aversion.

Supplementary motor area (SMA) activation was also found to positively correlate with strategic flexibility and performance when responding under a punishment contingency. The SMA has been implicated in determining whether or not to act (Karch et al., 2009), and its activation is possibly related to the role it plays in the preparation of voluntary motor action (Forstman et al., 2008). The positive correlation between SMA activation, strategic flexibility and task success may be related to better control over the motor system and better response execution, that is, pressing the intended button. It is also possible that, as a region implicated in determining future action, its greater activation reflects better transition from deciding to act to the action itself.

Posterior cerebellum activity decreased as strategic flexibility increased. The cerebellum has long been implicated in coordination and motor control. More recently, neuroimaging studies have found that it shows activation in a diverse set of cognitive and perceptual tasks (Cabeza & Nyberg, 2000). In a functional MRI study where participants had to choose between a small, immediate reward and a large, delayed reward, BOLD activation in the posterior cerebellum positively correlated with selection of the immediate reward (Boettiger et al., 2007; Boettiger et al., 2009). Interestingly, it was also found that lateral OFC activation correlated with selection of the large, delayed reward. In the present study, decreased

cerebellar activation and increased lateral OFC activation was correlated with strategic flexibility and success. The decrease in posterior cerebellar activation and the increase in lateral OFC activation, similar to Boettiger et al. (2007), suggest that greater strategic flexibility is related to a bias towards choosing larger, delayed rewards. It is possible that either greater strategic flexibility leads to this pattern of activation, or this pattern of activation results in adoption of a more flexible strategy.

The ventral posterior cerebellum is also highly connected to the DLPFC and has been implicated in automation of action (Ramnani, 2006). The present study found that strategic flexibility correlated with increased DLPFC activation and with decreased ventral posterior cerebellum activation. It is possible that decreased cerebellum activity reflects a disengagement from automatically implementing the current strategy's response rules. Activation of the DLPFC, an area long implicated in executive function, could then reflect the formulation and implementation of a new response strategy.

General Discussion

Through neuroeconomic studies, different components of the decision-making process are being identified and localised in the human brain. While it has become clear from these studies that there is a particular neural network consistently and predictably activated by the decision-making process, it has also become clear that there are activation differences within this network depending both on the personality of the individual and the decision-making strategy the individual adopts. For example, it has been demonstrated that individuals who are loss averse in financial decision-making tasks have a sensitised BOLD fMRI response, and in the present study it was demonstrated that the ability to employ strategic flexibility on a task was correlated with a differential BOLD response in several decision-making centres.

The study of neuroeconomics isn't just important for understanding the where and the how of decision-making; it also plays an important role in helping us understand both the deficits and the causes of particular psychopathologies. Decision-making deficits have been found in addiction (Reuter et al., 2005), major depressive disorder (Kaplan et al., 2006), panic disorder (Ludewig, et al., 2003), bipolar disorder (Minassian et al., 2004), and schizophrenia (Paulus et al., 2003; Moritz et al., 2005; Kim et al., 2007; Moritz et al., 2007; Polli et al., 2008) and seem to be related to differential brain activation patterns. The greater risk-seeking behaviour

shown by pathological gamblers in decision-making tasks correlates with decreased activation in the ventral striatum – a major reward and decision-making centre (Reuter et al., 2005). Patients with alcoholism show decreased ventral striatal activation to anticipation of monetary reward, but increased ventral striatal activation in response to alcohol associated cues (Wrase et al., 2007). Decision-making deficits in bipolar disorder seem to be related to prediction-error deficits. It was found that bipolar disorder patients in a manic state showed significantly less ventral striatal activation than healthy controls to omission of an expected reward (Abler et al., 2008). In a social decision-making game, patients with schizophrenia had altered patterns of activation in the orbitofrontal cortex and anterior insula cortex compared to controls (Baas et al., 2008). Similarly, patients with schizophrenia had significantly weaker ventral striatal activation than controls when the likelihood of having to inhibit a response increased (Vink et al., 2006). Decreased error-related activation in the anterior cingulate has also been found to characterise decision-making in patients with schizophrenia and has been suggested to play a role in their adoption of a more liberal response bias as well as contributing to their strategic inflexibility (Polli, et al., 2008).

While BOLD fMRI allows one to infer regions of activation based on changes in blood oxygenation, it does not allow for speculation on the underlying neurochemical basis of the observed changes; however, Positron Emission Tomography (PET) does. PET studies of addiction have shown that decreased dopamine functioning is associated with reduced activity in the ventral striatum, orbitofrontal cortex, and cingulate cortex – the same regions implicated in decision-making (Volkow et al., 2008). Similarly, increased DA transmission is associated with positive symptoms in schizophrenia (Kapur et al., 2005) – a disorder where patients have prominent decision-making deficits (Paulus et al., 2003a; Kim et al., 2007; Baas et al., 2008; Polli et al., 2008). From studies like these, it appears as if dopamine, decision-making and psychopathology are intertwined and that dopamine may play a role in individual differences in decision-making, and the decision-making deficits characteristic of certain psychopathologies.

Primate electrophysiological studies suggest that midbrain dopamine neurons release dopamine phasically and tonically (Schultz 1997; Schultz et al., 2008). It has been hypothesised that while phasic dopamine release codes the prediction-error component of decision-making (Schultz et al., 2008), tonic dopamine release codes for the uncertainty component (Fiorillo et al., 2003). It was found that tonic dopamine release followed an

inverted "U" function where midbrain dopaminergic response was strongest when uncertainty was greatest ($p = 0.5$), and was weakest when the outcome was certain ($p = 1$, or $p = 0$). This finding is mirrored in a human functional MRI study where activation in the prefrontal cortex (a ventral striatal projection site) followed the same inverted "U" function (Dreher et al., 2006). These findings suggest that dopamine could be responsible for the changes in BOLD fMRI activations when imaging the role of uncertainty in reward. Similarly, in humans, dopamine transmission has been related to the error-prediction component of decision-making (Pessiglione et al., 2006; Menon et al., 2007). These studies expose a possible link between dopamine and different components of the decision-making process. It is possible the observed individual differences in decision-making and BOLD fMRI activation, for example the finding that greater loss aversion is associated with relatively greater BOLD response in the decision-making network, could be a result of differences in dopamine transmission. This seems even more plausible when one considers that there are decision-making deficits in schizophrenia, a disorder where hyper-dopaminergic transmission in the midbrain and hypo-dopaminergic transmission in the frontal cortex is thought to respectively play a role in the positive and negative symptoms of the disorder (Davis et al., 1991). In drug addiction, with its own set of decision-making deficits, both fMRI and PET studies have shown that there are differential patterns of BOLD activation and of dopamine transmission in the ventral striatum, orbitofrontal cortex, anterior cingulate and anterior insula – the decision making network (Kilts et al., 2004; Risinger et al., 2005).

The differences in dopamine transmission that possibly underlie individual differences in decision-making may be the result of genetic variation amongst individuals (Yacubian et al., 2007; Schmack et al., 2008). Two of the genes that affect dopamine transmission are DAT which affects the dopamine re-uptake transporter, and COMT which affects the speed with which synaptic dopamine is degradated. Different allelic variations of COMT result in faster or slower degradation of synaptic dopamine. The most common genotype is homozygous for methionine ($MET^{158}MET$); however, valine (VAL) can be substituted for methionine resulting in either a genotype homogenous for valine ($VAL^{158}VAL$) or a heterozygous genotype. The different allelic variations affect the impact of synaptic dopamine. The homozygous valine genotype is four times more efficient at catabolising dopamine compared to the homozygous methionine genotype (Weinshilboum et al., 1999; cf. Yacubian et al., 2007). Similarly, individuals with a 9R DAT variant have fewer dopamine transporters in the

midbrain and more striatal dopamine than individuals with the 10R variant (Floresco et al., 2003; cf. Yacubian et al., 2007). While the link between genetics, dopamine and behaviour is not very well understood, it has been suggested that high PFC DA concentrations, as a result of low COMT activity, stimulates a descending glutamatergic projection which results in higher levels of tonic DA release in the ventral striatum (Yacubian et al., 2007). However, it has also been suggested that PFC dopamine activates intermediary GABAergic neurons that inhibit DA release from parts of the brain stem (i.e. VTA and substantia nigra) (Akil et al., 2003). In a BOLD fMRI study, differences in the COMT genotype resulted in differential activation in the ventral striatum and prefrontal cortex, while differences in the DAT genotype effected ventral striatal activation during anticipation of a monetary reward (Yacubian et al., 2007). This study demonstrated how genetic differences can influence dopamine transmission in regions of the brain implicated in the decision-making process.

CONCLUSIONS

Prospect theory stipulates that, in general, people weight losses more heavily than gains. However, it appears as if some people weight losses more heavily than others. From the results of the present study, I argue that it is greater relative sensitivity to financial loss that drives strategic flexibility – the more sensitive one is to loss, the more likely they are to adopt a flexible strategy to facilitate avoiding loss. Evidence from current literature suggests that individual differences in sensitivity may be driven by differences in dopamine transmission. In turn, differences in dopamine transmission appear to be driven by genetic variation. The use of a block design in the present study makes it ideal for use in a PET paradigm where the link between dopamine transmission, genetics and decision-making can be investigated. Further, since abnormalities in both decision-making and dopamine are characteristic of many different psychopathologies, the present paradigm could be used in both PET and fMRI imaging to investigate the relationship between decision-making deficits and strategic flexibility.

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APPENDIX A

UNIVERSITETET I OSLO

TOP

ULLEVÅL universitetssykehus

Vil du være med i en fMRI-studie av hjernen?

Vi skal undersøke hvilke hjerneområder som er involvert i belønning ved å benytte funksjonell magnetisk resonans.
Undersøkelsen blir gjort i en MR-maskin. Du må totalt sette av ca to timer fordelt på to dager, og du får betalt for å delta.
Hvis du er interessert i å delta eller har spørsmål om studien, kan du kontakte Ingeborg Bolstad:
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Husk å oppgi ditt telefonnummer.